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DISSEMINATED BLASTOMYCOSIS.

REPORT OF A CASE INVOLVING THE LUNGS, LUMBAR VERTEBRÆ, AND SUBCUTANEOUS TISSUES, WITH MULTIPLE ABSCESES AND FISTULÆ, AND EXTENSIVE AMYLOID DEGENERATION.*

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THE CLINICAL RECORD.†

G. S., a boy 17 years old, entered the service of Dr. Senn in the Presbyterian Hospital on July 26, 1904. Both parents are living and in good health. A sister nine years old is living and well. Four brothers and sisters died during infancy or early childhood. No history of any form of tuberculous trouble in any member of the family can be obtained from the patient. The patient is a native of Chicago, and has lived in the neighborhood of Haymarket Square, Chicago, doing any kind of work he might pick up. He had measles and mumps in childhood, later gonorrhea. The history of the ailment for which he sought admittance to the hospital reads as follows: "In March of this year (1904) he slipped and fell, striking on the right shoulder. The next day the shoulder was lame and he went to a doctor, who told him that he had a sprain, and put on a plaster dressing. There was at that time some swelling and considerable pain which later partly disappeared. Since April the swelling has been stationary and painless except on pressure. The patient states that for some time previous to this trouble he had pain throughout the whole lumbar region, and a gnawing sensation in the upper part of the right lung, and that he has lost 30 pounds in weight. He coughs considerably and has night-sweats." The temperature on the day of admittance was 99.8°, pulse 100, respiration 20. On the same day (July 26, 1904), a trocar was passed into a large abscess over the right scapula and about one ounce of thick, slightly blood-stained pus was evacuated. Iodoform emulsion was injected and the wound sealed with collodion. The urine was normal. During the following week the temperature rarely exceeded 100° (maximum 100.2°). On August 2, the abscess over the scapula was opened by a transverse incision 3.5 inches long, scraped out, and packed with iodoform gauze. During the week following the temperature on several occasions reached 102°. August 9, a large abscess in the right lumbar region was freely incised and one pint of pus evacuated. During the following two months there was a daily rise in temperature to 100° or 101°, the pulse commonly fluctuating between 64 and 112. The respirations were not accelerated. September 1 a blood count revealed 4,180,000 erythrocytes and 19,500 leucocytes. Blastomycetes were repeatedly found in smears of pus from the various subcutaneous abscesses. Later they were also found in the sputum, never in the feces. Pure cultures of blastomycetes from the pus were obtained by

* Received for publication December 28, 1905.

† For permission to quote from the Hospital records, I am indebted to Dr. E. J. Senn.

Dr. R. H. Goheen, who also successfully inoculated guinea-pigs and recovered the organisms from them.*

The patient was discharged improved on November 15 with a diagnosis of blastomycosis, and readmitted on December 18, 1904. The temperature during the first two weeks generally ran between 100° and 103°. Nausea and diarrhea were present at times. On January 3, 1905, abscesses in the right scapular and in the lumbar region were incised. The irregular fever continued. A leucocyte count of January 25 was 1,760, hemoglobin 50 per cent. He frequently complained of pain in the back and right shoulder and of nausea with occasional vomiting. In May repeated examination of the urine revealed a large quantity of albumin with hyaline and granular casts; 1,600 c.c. of specific gravity 1.012 were voided in 24 hours. The reaction was alkaline. Blood pigment and red cells were found. During the last two months of the patient's life diarrhea was constant and gradually increased in severity. The limbs became edematous and painful. Abdominal pain was frequent. The irregular fever persisted and the patient gradually became weak. The temperature was subnormal the last four days of the patient's life. Death occurred on June 27, 1905.

SUMMARY OF THE RESULTS OF THE GROSS AND MICROSCOPIC EXAMINATION AFTER DEATH.

Chronic subcutaneous blastomycetic abscesses in right scapular region and in loin; abscess and sinus walls made up of vascular granulation tissue rich in polymorphonuclear leucocytes, mast cells, and blastomycetes. Blastomycotic caries of fourth and fifth lumbar vertebræ, with bilateral psoas abscesses. Disseminated blastomycotic broncho-pneumonic foci in both lungs. Areas of necrosis with Langerhans giant cells in the mediastinal glands. Amyloid degeneration of spleen, liver, adrenals, retroperitoneal, mesenteric and mediastinal lymph nodes, kidneys and colon.† Bilateral fibrinous pleuritis, and mild sero fibrinous peritonitis. Chronic parenchymatous nephritis. Atrophy of the heart. Pulmonary edema. Edema of feet and thighs. Tigrolysis of ganglion cells of cerebral cortex and ventral horns of cord (only upper cervical portions of latter examined).

THE NECROPSY RECORD.

The necropsy was held by the writer six hours after death. The following record was made:

The body is that of an emaciated young man with long, slim neck and slender bony development. Rigor mortis is present. The lower extremities are flexed at the knees at an angle of about 145 degrees, and cannot be extended without considerable force. There is edema of both feet and slight edema on the inner aspect of both thighs. Below the spine of the right scapula is a defect in the skin 5.5 cm. from above downward,

* Dr. Goheen is now abroad, and I have been unable to learn further details of his work. His records and specimens unfortunately are not now available.

† Mentioned in order of severity; slight in colon.

and 4 cm. from side to side. The inner border is 4.5 cm. to the right of the median line. At the inner border of the scapula are two openings each about 1 cm. long. Through the lower opening a probe passes upward and inward for a distance of 1 cm. before meeting any resistance. Through the upper opening it passes upward to the inner border of the scapula just beneath the skin, for a distance of 6 cm. In laying the upper sinus open, it is found to have a smooth shiny lining, with a small amount of liquid secretion. The lower sinus has a similar lining; it ends just behind the clavicle. There is apparently no connection with the chest cavity. There is another opening on a level with the crest of the ileum, and 6 cm. to the right of the median line of the back. Through this sinus a probe is passed outward for a distance of 7 cm. The sinus ends blindly at the crest of the ileum, in the subcutaneous tissue just above the crest. From the middle of the sinus a narrow opening passes inward, and a probe may be passed 5.5 cm. in the direction of the abdominal cavity. Six cm. to the left of the median line of the back, and 2 cm. lower than the above, is another smaller opening discharging whitish pus. Through this opening a probe passes 5 cm. in the direction of the abdominal cavity.

Very little subcutaneous fat is present.

The peritoneal cavity contains about 100 c.c. of turbid, grayish fluid, rich in fibrinous flakes. The peritoneal surfaces are smooth, and are not hyperemic anywhere. There are no abnormal adhesions. The diaphragm reaches to the fourth interspace on each side.

The left pleural cavity is free from adhesions, and contains about 200 c.c. of cloudy, yellowish fluid. The right pleural cavity is partly obliterated by fibrous adhesions, and contains about 200 c.c. of fluid which is more cloudy than that of the left side.

Each lateral lobe of the thyroid measures 3.5 x 1.5 cm. The cut surfaces are uniformly pale and gelatinous.

The cervical lymph nodes are not enlarged. The nodes in the mediastinum are moderately enlarged, measuring 1.5 cm. in length, and whitish nodules are seen on the cut surfaces. The tracheo-bronchial nodes are of similar size, and are anthracotic, but contain no nodules.

The larynx and trachea have a smooth and pale lining.

The left lung weighs 230 gms. The pleura is smooth and bluish gray. In the surfaces of both lobes numerous shotlike elevations are seen. On palpation both lobes are found to be studded with hard nodules. On the external surface the elevations are yellowish in the middle, surrounded by a bluish-red zone. On section the nodules are also seen to possess a grayish center surrounded by a hyperemic zone. Grayish-white pus can be expressed from the center of many of the nodules. The lung tissue between the nodules crepitates and contains a considerable amount of watery frothy fluid.

The right lung is larger than the left. It weighs 420 gms. All lobes are studded externally by nodules, that average about 3 mm. in diameter (Fig. 1). The cut surfaces of the upper and middle lobes resemble those of the left lung. The lower lobe contains more blood and frothy fluid, and the large bronchi contain bloody mucus.

The heart is small, weighing 180 gms. The epicardium is smooth. The tricuspid opening admits six finger-tips, the mitral four. The endocardium shows no changes. The myocardium is uniformly light grayish-red.

The aorta is smooth.

The spleen weighs 220 gms. It is firm, the capsule tense, the surface shiny. The cut surface is of a translucent, grayish-red color, the Malphigian bodies being large, transparent, and gray. On treatment with Lugol's solution, a typical amyloid reaction is obtained.

The tongue, pharynx, and esophagus are smooth.

The stomach is small, measuring 15 cm. from side to side and 5 cm. from above downward. The lining is smooth with numerous minute ecchymotic spots. The rugæ are prominent.

The small intestines are smooth, the mucous membrane thin and the lymphatic structures small.

The large intestines also have a smooth lining.

The liver weighs 1,550 gms. It is smooth externally and firm. The cut surface has a smooth, glistening, bacony appearance. The lobular markings are fairly distinct. The central portions are light grayish-brown; the outer portions are pale gray. No nodules are seen. On treatment with Lugol's solution typical amyloid reaction is obtained.

The gall-bladder is rather small, and contains thick, fluid bile.

The pancreas weighs 90 gms. It is rather firm and pale. The lobular markings are distinct.

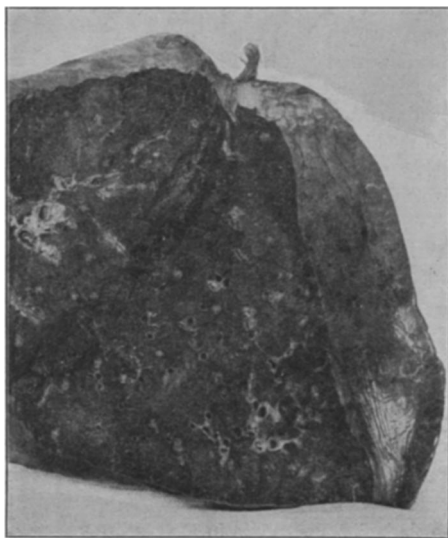


FIG. 1.—Right lung, showing nodules on cut and external surfaces.

The adrenals are of normal size. Their cortical portion is rather thick and glistening, and gives the amyloid reaction with iodine. A few pin-head-sized grayish nodules may be seen in the surfaces of both organs.

The kidneys together weigh 340 gms. The capsule strips readily, leaving a pale, gray surface, on which the stellate veins are prominent. The cut surface is pale gray with indistinct markings; numerous vessels are plainly seen. The cortex is 8 mm. thick; the pelvis is smooth. Both kidneys answer the same description.

The ureters are of normal caliber.

The urinary bladder has a smooth and pale lining.

The prostate is rather small. The cut surface is uniformly white. The seminal vesicles are not altered.

The testicles are rather small. The cut surface is pale gray.

The periaortic lymph nodes are small, the largest measuring 1 cm. in length. They are pale gray on cut sections.

The mesenteric nodes are slightly enlarged, measuring about 1 cm. in length.

On examining the lumbar vertebræ, two openings communicating with the sinuses described in the soft parts of the back are found to lead into necrotic bone tissue. The

necrosis has involved the adjacent parts of the body of the fourth and fifth lumbar vertebræ, and partly destroyed the intervertebral disk, which is replaced by grayish-white, soft necrotic tissue. A considerable amount of grayish pus is present and is found to have burrowed along the sheaths of both psoas muscles, forming suppurating sinuses lined by whitish tissue resembling that lining the subcutaneous sinuses. The pus has burrowed downward to the trochanters, but here both sinuses end blindly. No changes are found in other parts of the spine, or in the right scapula underlying the ulcerated skin described.

The right knee-joint and lower part of the right femur show no changes.

The skull, scalp and dura mater show no changes.

The brain shows no external change. Only the upper part of the spinal cord was removed.

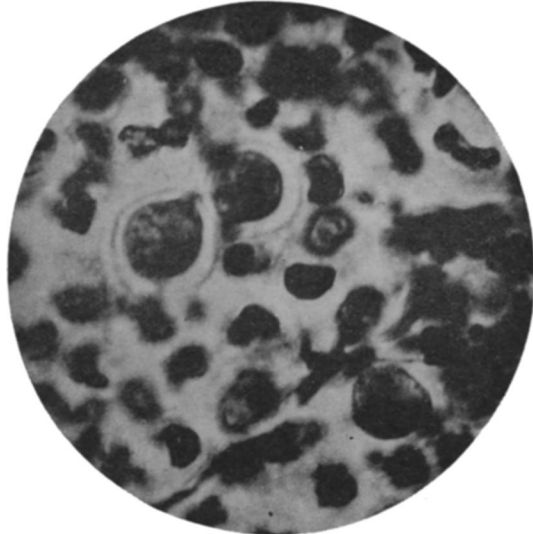


FIG. 2.—Photomicrograph. About $\times 1000$. From the lining of the sinus over the right scapula. Two organisms are seen. Polychrome blue stain.

STUDY OF SMEARS AND CULTURES.

The efforts to cultivate blastomycetes failed, though numerous such organisms were seen in cover-glass preparations of bronchial mucus, of pus from the carious vertebræ, and of pus from the sinuses about the shoulder and loin. Two sets of pipettes were filled with material from the autopsy, and smears and cultures were made independently by Dr. S. A. Berg, and myself. In the main similar colonies were obtained by both of us, and the work of identification of the organisms from both sets was finally carried out by Dr. Berg.

Pericardial fluid.—Smears show no organisms. Cultures sterile.

Right pleural fluid.—Endothelial cells containing fat globules and fatty acid crystals in the smears; no organisms. Colon bacillus in the cultures.

Left pleural fluid.—Smears show cocci; polymorphonuclear cells. Cultures gave *Staphylococcus aureus* and *albus*.

Peritoneal fluid.—Short bacilli in the smears also endothelial cells with fat globules. Colon bacillus in cultures.

Heart's blood.—The colon bacillus and a streptococcus developed late on some of the tubes and plates.

Bile.—Smears and cultures; no organisms.

Bronchial secretion.—Blastomycetes in smears; also cocci. *Staphylococcus aureus* in cultures.

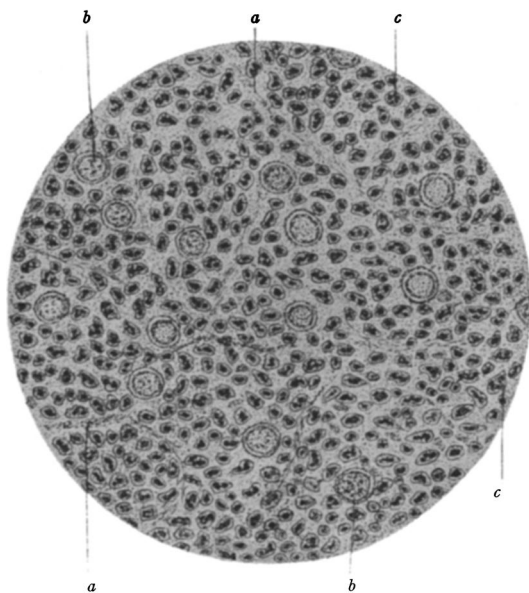


FIG. 3.—Drawing from a nodule in the lung. *a*, Alveolar walls; *b*, Blastomycetes; *c*, Polymorphonuclear cells.

Smears of pus from sinus in left loin showed blastomycetes, many of which are budding. Cultures gave the colon bacillus.

Lung emulsion.—Blastomycetes and cocci in smears. Cultures gave *Staphylococcus aureus* and colon bacillus.

Spleen emulsion.—No organisms in smears. Cultures showed *B. pyocyaneus* (contamination?).

Liver emulsion.—Smears and cultures sterile.

Kidney emulsion.—Smears showed no organisms. Cultures gave *B. pyocyaneus* and a pigment-producing bacillus (contamination?).

HISTOLOGICAL EXAMINATION.*

Subcutaneous lesions.—Pieces from the ulcerated tissue overlying the scapula were fixed in formalin and stained with hematoxylin-eosin and polychrome blue. There is a large amount of vascular granulation tissue of usual appearance. Many mast cells are seen. Blastomycetes are very abundant, and in two places they are seen within the lumina of blood-vessels. The organisms are of typical appearance, spherical with double contour (Fig. 2). They contain a variable number of large granules stained blue or brownish with polychrome blue. The central portion of the organism as a rule is homogeneous. Several budding forms are seen. In places the granulation tissue also contains numerous long slender bacilli and clusters of cocci.

Sections from the lining of one of the sinuses in the loin show muscle lined by granulation tissue, in which a few blastomycetes are seen. The endothelial cells are seen. The endothelial cells of the vessels are tall. Polymorphonuclear cells and cocci are abundant. A few bacilli are seen.

* When not otherwise stated fixation by Zenker's fluid and 95 per cent alcohol has been used, and staining by hematoxylin-eosin, polychrome methylene blue, and Loeffler's alkaline methylene blue.

Lungs.—Sections were made from many portions of both lungs. In the nodular areas the alveoli are filled with inflammatory cells, among them many polymorphonuclears. In the central portion of the areas the alveolar outlines are generally lost, and in places necrosis has taken place. In the outer portions the alveolar outlines are distinct, and the alveoli are chiefly filled with desquamated epithelial cells, leucocytes, and red cells. There are also extensive hemorrhages in the interior of the nodules. Blastomycetes are abundant (Fig. 3) in all parts of the consolidated areas, and occasionally show budding. Many bronchi are filled with a detritus in which numerous large bacilli, many cocci, and occasionally blastomycetes, are found. In the walls of such bronchi mast cells are plentiful; such cells are also occasionally seen about the vessels. In a large number of sections examined, only one giant cell was found. This is located in a partly necrotic nodule, and is of the Langerhans type. No tubercle bacilli are found in sections stained by carbolfuchsin in the usual manner.

Lumbar vertebrae.—A piece which included the intervertebral disc between the two affected vertebrae was fixed in Zenker's fluid, and subsequently decalcified with nitric acid. The cartilage was partly destroyed and covered by a

fibrinous exudate in which pieces of necrotic cartilage and bone are embedded. In the meshes of this exudate blastomycetes are extremely abundant, more so than in any other part of the body from which sections were made (Fig. 4). Numerous blastomycetes are also seen throughout the spongy bone, in one instance within a giant cell (see Fig. 5). In this region the cells of the spongy substance are much more densely packed than in the interior, and the proportion of polymorphonuclear cells is greater.

Lymph nodes.—*a)* Mediastinal. In sections from one of these, areas of necrosis are seen. A few giant cells of the Langerhans type, plasma cells, and occasionally mast cells, are found. No blastomycetes are seen. Several sections were stained for tubercle bacilli with negative results. Portions of the node are affected by amyloid degeneration.

b) Mesenteric. Here the amyloid change is more marked. Numerous polymorphonuclear cells are seen among the lymphoid cells. There are no areas of necrosis, and no blastomycetes are seen.

c) Retroperitoneal. The amyloid degeneration is considerably more advanced

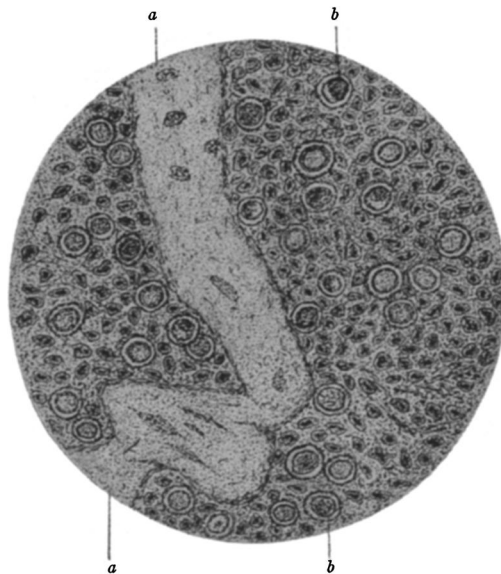


FIG. 4.—Drawing from section of lumbar vertebra. *a*, Necrotic bone; *b*, Blastomycetes.

than in the mesenteric nodes. Polymorphonuclear cells are very abundant; there is proliferation of endothelial cells, and numerous mast cells are seen. No blastomycetes are found in a large number of sections examined from various lymph nodes. Bacilli are present in sections stained with methylene blue.

In the *liver*, and in the *spleen* even more so, the amyloid degeneration is marked. The spleen is a typical "sago" spleen.

The *adrenals*, particularly the middle zone of the cortex, are distinctly amyloid.

In the *kidney* most glomeruli present slight amyloid change in their capillaries. The convoluted tubules, as a rule, are slightly dilated, and contain granular detritus;

their epithelial cells in many places are degenerated. There is no increase in interstitial tissue.

The digestive tract.—The tongue and stomach are not materially altered. In the ileum there is extensive necrosis of the mucous membrane. Numerous large bacilli are seen, but leucocytes are very scarce. The walls of many of the small vessels in the mucosa are thickened and homogeneous. In the colon the change is more marked.

There are no noteworthy changes in the *thyroid*, *myocardium*, *prostate*, and *testicle*.

The nervous system.—In Nissl specimens from the paracentral lobules well-marked tigrolysis is present. In the Betz cells the tigroid appears as if finely pulverized in the center of the cells and

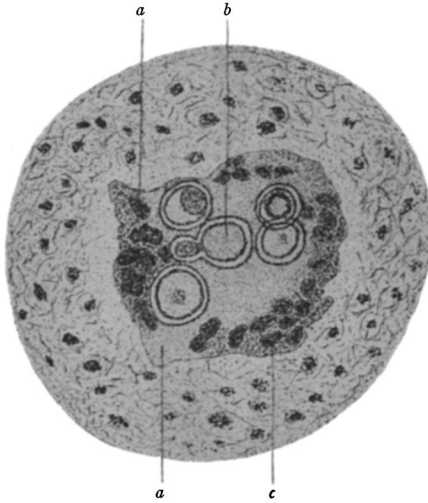


FIG. 5.—Drawing from section of lumbar vertebra showing a giant cell. *a*, Cytoplasm of giant cell; *b*, Blastomycetes (one budding); *c*, Nuclei of giant cell.

as coarse granules along the periphery. Distinct Nissl bodies are found in the dendrites only. The nucleus is frequently peripherally located with ill-defined outline and chromatin network. The dendrites are visible for a long distance. Tigrolysis is also seen in the pyramidal cells of the frontal lobe, and to a lesser extent in the ventral horn cells.

REMARKS.

This is the fifth case of general infection with blastomycetes to be reported from Chicago since 1902.

The first Chicago case was that of Walker and Montgomery¹ in which primary blastomycetic dermatitis was followed by general dissemination which at the necropsy was mistaken for miliary tuberculosis.

¹*Jour. Am. Med. Assoc.*, 1902, 38, p. 867.

In the second case, that of Ormsby and Miller,¹ the lungs appear to have been primarily attacked. At the autopsy lesions were also found in the skin, subcutaneous tissues, liver, spleen, kidney, pancreas, and trachea. Amyloid changes in the kidney are described. A further study of the organisms in this case is found in an article by Otis and Evans.²

In 1904 Cleary³ reported a case in which also the lungs appear to have been primarily involved. Other lesions were found in the cervical nodes, liver, kidneys, spleen, myocardium, and adrenals. There was amyloid degeneration of the spleen, kidneys and adrenals.

In 1905 Eisendrath and Ormsby⁴ reported the case of a man, 33 years old and still living, in whom pulmonary symptoms existed for four months prior to the appearance of cutaneous and subcutaneous lesions. Blastomycetes were found in the sputum. It is a point of great interest that in this patient symptoms of spondylitis recently developed.

The present and fifth Chicago case is very likely also one of primary infection of the lungs, although the history of the onset is not clear. It is the first one in which spondylitis due to blastomycetes, with psoas abscess, has been demonstrated postmortem.

In addition to these five cases the writer knows of several which have been observed in Chicago or vicinity within the past year, and hopes they will soon be placed on record in as detailed a form as possible. A complete case report of generalized blastomycosis does not yet exist. Either the history or the symptomatology, or the microbiologic work during life or after death, or the details of the necropsy, have been more or less defective. Careful recording of details in many cases will be necessary before the clinical and anatomical "textbook" picture of blastomycosis can be drawn.

As yet the organisms concerned have not been placed definitely and it is not now possible to differentiate between the essential and the non-essential in their variable biologic characteristics. For this reason no attempt is made at this time to correlate these five

¹ *Jour. of Cut. Dis.*, 1903, 21, p. 121. ² *Jour. Am. Med. Assoc.*, 1903, 41, p. 1075.

³ *Trans. Chicago Path. Soc.*, 1904, 6, p. 105; also *Medicine*, 1904, 19, p. 818

⁴ *Jour. Am. Med. Assoc.*, 1905, 45, p. 1045.

Chicago cases—all of which apparently are due to very similar organisms—and the few similar cases reported elsewhere. Very likely the previous recorders of cases from Chicago are right when they consider the case reported in Germany by Busse¹ and Buschke² to belong to the same class. The only difference between the organism from this case and those from the Chicago cases seems to be that the former did not produce aerial hyphæ. With our present insufficient botanical knowledge it also is impossible to give an opinion on the relation of these cases to the 13 cases which recently have been collected by Ophüls³ under the title of "coccidioidal granuloma." Besides many new ones from California, Ophüls includes the well-known and frequently discussed cases of Posadas and Wernicke,⁴ Rixford and Gilchrist,⁵ and that of Ophüls and Moffitt.⁶ In all of these cases the organisms are characterized by the absence of budding during their development in the tissues and by their multiplication by endosporulation. Clinically the cases very much resemble the Chicago cases and like the latter they also resemble tuberculosis. Ophüls makes the statement that in infection with blastomycetes the primary focus is always in the skin, whereas in the so-called coccidioidal granuloma it is just as likely to be found elsewhere. This point loses its value when we analyze the five Chicago cases, in only one of which (that of Walker and Montgomery) was the primary focus in the skin. Skin lesions were found in six of Ophüls' 13 cases and considered primary in four cases. Bone lesions, frequently multiple, and strongly resembling tuberculous caries, were found in six of the cases. Multiple bone lesions also existed in the Busse-Buschke case.⁷

I have used the term "blastomycosis" with considerable misgiving, as I am aware that there is a tendency among botanists to designate as "blastomycetes" the budding forms of any fungi which

¹ *Virch. Archiv*, 140, p. 23, and 144, p. 360.

² Volkmann's *Samml. klin. Vorträge*, 1898, 218; also *Verhandl. d. Deutsch. dermat. Gesellsch.*, 1899, p. 181.

³ *Jour. Am. Med. Assoc.*, 1905, 45, p. 1291.

⁴ *Centralbl. f. Bakt.*, 1892, 12, p. 859.

⁵ *Johns Hopkins Hospital Reports*, 1896, 1, p. 209.

⁶ *Phil. Med. Jour.*, 1900, 5, p. 1471.

⁷ A case of myxoma-like tumor in the thigh and deep abscesses due to a yeastlike organism is reported by Curtis (*Ann. de l'Inst. Pasteur*, 1896, 10, p. 449). This case and all other cases of infection with blastomycetes and allied organisms reported up to 1900 are abstracted and thoroughly discussed in the monograph by Ricketts "Oidiomycosis of the Skin and its Fungi," *Jour. Med., Res.* 1901, 1, p. 373.

otherwise may not at all belong together. For the present the term "blastomycosis" is used for lack of a better one and in order to emphasize the fact, so important from a medical standpoint, that we are dealing here with an infection by organisms which bud in the tissues of the human body.